

## REMARKS/ARGUMENTS

After entry of this paper, claims 12-16, 18, and 31-39 are pending. Claim 31 is amended to specify that the antioxidant comprises d,l- $\alpha$ -tocopherol. Claims 14, 32, and 35 are amended in view of the amendment made to claim 31. Claims 38 and 38 are amended for clarification. These amendments are supported in the specification on page 4, lines 24-29. No new matter is added by these amendments.

### **35 USC § 112, Second Paragraph Rejection**

*Claims 38 and 39 are rejected under these section and paragraph. The Examiner alleged that the placement of commas and semicolons makes it appears as though the concentration of CCI-779 is with regard to the dehydrated ethanol alone.*

Applicants respectfully request reconsideration of this rejection for the following reason.

Solely in an effort to expedite allowance of this application, claims 38 and 38 are amended to utilize commas instead of semicolons to separate the components of the formulations. These amendments clarify that the concentration of CCI-779 is not related to the dehydrated ethanol.

Withdrawal of this rejection is requested.

### **35 USC § 103(a) Rejection**

*Claims 12-16, 18, and 31-39 are rejected under this section over Skotnicki (US Patent No. 5,362,718) in view of Waranis (US Patent No. 5,516,770) and Haeberlin (Great Britain Application Publication No. 2,327,611).*

*The Examiner alleged that it would have been obvious to combine the teachings of Skotnicki which discusses hydroxyester rapamycin derivatives and formulations thereof, with Waranis and Haeberlin which teach rapamycin formulations.*

*The Examiner asserted that "...it is not inventive to discover the optimum or workable ranges by routine experimentation when general conditions of a claim are disclosed in the prior art."*

*The Examiner made the following statements to support the outstanding rejection:*

- *Haeberlin* discusses the instability of macrolides upon storage and formulations with citric acid and d,l- $\alpha$ -tocopherol to rectify the problem
- CCI-779 is one of the compounds claimed in *Skotnicki* in claim 13 - this would have provided ample motivation to select CCI-779 from the reference.
- *Haeberlin* teaches rapamycin formulations with d,l- $\alpha$ -tocopherol on page 6 and it is inherently an antioxidant.

Applicants respectfully request reconsideration of this rejection for the following reasons.

Contrary to the Examiner's assertion, a prima facie case of obviousness can properly be rebutted by showing that there are new and unexpected results relative to the prior art<sup>1</sup>, the claimed range achieves unexpected results relative to the prior art range<sup>2</sup>, and/or the prior art teaches away from the claimed invention.<sup>3</sup> On pages 5-6 of Applicants' Response filed on December 2, 2008, Applicants did just that. Specifically, Applicants noted that *experimental evidence was* generated by the assignee and is provided in Example 3 of US Patent Publication No. US-2007/0142422. This evidence shows that CCI-779 compositions containing higher concentrations of d,l- $\alpha$ -tocopherol, *i.e.*, 1%, resulted in an increase in oxidative impurities as compared to compositions containing lower concentration of d,l- $\alpha$ -tocopherol, *i.e.*, 0.2 and 0.5%. Applicants also discussed that their finding is ***counter to what is known and would be expected in the art***

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<sup>1</sup> MPEP page 2100-153 citing *Iron Grip Barbell Co., Inc. v. USA Sports, Inc.*, 392 F.3d 1317, 1322, 73 USPQ2d 1225, 1228 (Fed. Cir 2005)

<sup>2</sup> MPEP page 2100-152 citing *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990)

<sup>3</sup> MPEP page 2100-152 citing *In re Geisler*, 116 F. 3d 1465, 1471, 43 USPQ2d 1362, 1366 (Fed. Cir. 1997).

*regarding antioxidants.* The Examiner erroneously disregarded this experimental evidence and that the same teaches away from what is known and would be expected in the art. This is not permitted under US patent law.

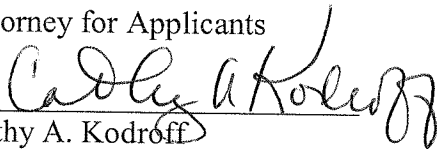
"The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art".<sup>4</sup> However, Applicants have clearly shown that one of skill in the art **would not** be able to combine the cited Skotnicki, Waranis, and Haeberlin cited documents to result in Applicants' invention of the pending claims. Specifically, the combination of Skotnicki, Waranis, and Haeberlin does not suggest that a composition containing **more d,l- $\alpha$ -tocopherol antioxidant** would result in compositions containing more oxidative impurities or that a composition containing **less d,l- $\alpha$ -tocopherol antioxidant** would result in compositions containing fewer oxidative impurities.

In view of these comments and minor claim amendments, withdrawal of this rejection is requested.

The Director is hereby authorized to charge any deficiency in any fees due with the filing of this paper or during the pendency of this application, or credit any overpayment in any fees to our Deposit Account No. 08-3040.

Respectfully submitted,

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<sup>4</sup> MPEP page 2100-140 citing *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 127 S. Ct. 1727, 82 USPQ2d 1385, 1396 (2007)